

REMARKS

Claims 1 and 13 have been amended to more definitely set forth the invention and obviate the rejections. In addition, new claims 17-33 have been added to claim a method of measuring antioxidant properties of a composition when applied to skin. Support for the amendments of claims 1 and 13, as well as new claims 17-27, can be found in the Specification on page 5, in the "Summary of the Invention" section. Support for new claims 28-33 may be found in the Specification on page 20, line 20, to page 22, line 23, Example 7 on pages 34 and 35, and in Figure 4. This amendment is believed not to add new matter. Claims 1-4 and 13-33 are now in the application.

Reconsideration is respectfully requested of the rejection of claims 1-4 and 13-16 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1 and 13 have been amended to clearly state which metabolic intermediates of sulfur containing amino acids are included in the Markush group. In addition, claims 1 and 13 have been amended to include thiotaurine and hypotaurine in said Markush groups.

Further, claims 1 and 13 have been amended to more clearly define what is included in the Markush group as stated in lines 17-21 thereof.

With regards to claims 2 and 14, the Examiner's interpretation of same, as stated in paragraph 9 on page 3 of the Office Action is correct in one respect. Namely, claims 2 and 14 should be interpreted to mean that when a sulfur containing amino acid is present it must be glutathione, and when a metabolic intermediate of a sulfur containing amino acid is present it must be either thiotaurine or hypotaurine.

However, in view of the amendments to claims 1 and 13 herein, claims 2 and 14 do now require that both glutathione AND either thiotaurine or hypotaurine be present in the composition used in the presently claimed method.

In view of the amendments to claims 1 and 13 made herein, as well as the comments provided above, it is believed that the rejection is now moot. Withdrawal of the rejection is accordingly respectfully requested.

Reconsideration is respectfully requested of the rejection of claims 1, 2, 13 and 14 under 35 U.S.C. 102(a), as being anticipated by Egawa, et al., Cigarette smoke induced lipid peroxidation and its oxidative effect on the skin, 3<sup>rd</sup> ASCS Conference, Taipei, Taiwan, (1997), pages 217-276.

The cited presentation and the scientific paper associated therewith have a publication/presentation date of **May 23, 1997**, as evidenced by the attached copy of same. The present invention, however, is a division of parent application serial No. 09/478,882, filed January 7, 2000, itself a Continuation-In-Part application of parent U.S. patent application serial No. 09/147,293 filed November 23, 1998. This parent application serial No. 09/147,293 claims a priority date of **March 30, 1997**, based upon a Japanese priority application No. 9/95307, the benefit of which the present application is entitled to.

Thus, based upon the foreign priority date of March 30, 1997, which is almost 2 months prior to the publication/presentation date of the cited reference, it is believed that the cited Egawa, et al. reference fails to constitute as prior art. Thus, withdrawal of the rejection is accordingly respectfully requested.

Reconsideration is respectfully requested of the rejection of claims 1, 2, 13 and 14 under 35 U.S.C. 102(a) as being anticipated by US 5,601,806 ('806).

The cited '806 reference is concerned with methods for scavenging (eliminating) active oxygen compounds and preventing damage from ultraviolet B rays (UVB) using taurine and its analogues, especially aminothiosulfonic acids. In particular,

Katsumata, et al, were concerned with mimicking the function of superoxide dismutase (SOD), a naturally occurring substance in the body which decomposes and detoxifies superoxides caused by exposure of the skin to UVB radiation (see column 3, last paragraph).

In particular, Katsumata, et al. disclose that thiotaurine, the main component of the cited reference, destroys superoxides, singlet oxygen and peroxide (see Experiments 1 and 4). Further, the oxidation of oil is disclosed. If during such oxidation thiotaurine is present, thiotaurine prevents oxidation of oil and amino acids. However, oxidation of such components is caused ALSO by free radicals, of which there is no mention or disclosure in the cited '806 reference.

Furthermore, in contrast to the disclosure of Katsumata, et al. concerning preventing oxidation of certain elements in the skin caused by exposure of the skin to UVB radiation, the present invention provides a *method for treating environmental stress on the skin due to contact of the skin with tobacco smoke by suppressing reduction in corneum moisture content caused by contact of the skin with tobacco by applying the liniment claimed herein, and a method of treating environmental stress due to exposure of the skin to tobacco smoke by suppressing ultraweak chemiluminescence using the same procedure.* Such methods, as

claimed herein, are neither disclosed nor suggested by Katsumata, et al., and constitute important elements or aspects of the present invention.

A method of measurement of such environmental stress caused by contact of the skin to tobacco smoke was unexpectedly discovered by Ms. Egawa, one of the present inventors, utilizing measurement of chemiluminescence (CL) in the skin, as well as corneum moisture content. Such unexpected discovery of the effects of tobacco smoke upon contact with the skin, the causes associated with the above mentioned environmental stress (which includes oxidation), and experimental data associated therewith, are discussed in the attached scientific paper entitled "Oxidative Effects of Cigarette Smoke On The Human Skin", the authors of which include the present inventors Ms. Egawa and Mr. Kohno.

It was found that CL arises mainly from the decay of excited states generated during a chemical reaction, in this case oxidation caused by exposure of the skin to floating fine particles contained in tobacco smoke. The active species unexpectedly discovered by the present inventors to be related to CL include singlet oxygen, excited carbonyls and excited carbonic acid, which, upon exposure to free radicals contained in the tobacco smoke, become excited and chemiluminesce. This unexpected

discovery (the prevention of free radicals contained in tobacco smoke from oxidizing the skin by applying the composition claimed herein) is in no way disclosed or suggested by the cited '806 reference, and constitutes an important element or aspect of the present invention.

Further, the present inventors have unexpectedly discovered that, by measuring the chemiluminescence, *in vivo*, of human skin the oxidation thereof by external forces, such as UV radiation and the like, can be measured. Such a discovery provides a valuable method of screening/determining which chemical compounds may most effectively inhibit oxidation of the skin, as now claimed herein newly presented claims 17-. For example, researchers may utilize such method to accurately and economically discover new antioxidants/protectants by applying various medicants to the skin *in vivo*, and measuring the resulting chemiluminescence thereof when exposed to UV radiation.

In contrast, the '806 reference merely discloses that thiotaaurine destroys active oxygen *in vitro*. There is no disclosure whatsoever of the relation of chemiluminescence to oxidation of the skin, as was unexpectedly discovered by the present inventors.

In view of the deficiencies of the cited '806 reference discussed above, it is believed that the Examiner would be

justified in no longer maintaining the rejection. Withdrawal of the rejection is accordingly respectfully requested.

Reconsideration is respectfully requested of the rejection of claims 1-4 and 13-16 under 35 U.S.C. 102(e) as being anticipated by US 5,747,049 ('049).

The cited '049 reference has an effective date of **May 5, 1998**, whereas the present application has a foreign priority date of March 30, 1997. As required by 37 C.F.R. 1.55, and in accordance with the Examiner's comments on page 4, paragraph 13, of the instant Office Action, an English translation of said foreign priority document is attached hereto.

It is believed the presentation of said English translation, and the claim for benefit of foreign priority thereof, entitles the applicants to claim an effective filing date prior to the effective date of the cited reference. Thus, it is believed that the cited '049 reference is inapplicable as prior art in the instant application. Withdrawal of the rejection is accordingly respectfully requested.

Reconsideration is respectfully requested of the rejection of claims 1-4 and 13-16 under 35 U.S.C. 103(a) as being unpatentable over either US 5,747,049 ('049) or US 5,601,806 ('806) in view of Egawa, et al.

As discussed above, it is maintained that neither the cited

'049 reference nor the cited Egawa, et al. reference qualify as prior art in the instant application. Furthermore, it is believed that, in the absence of the benefit of the teaching of the Egawa, et al. reference with regards to prevention of damage to the skin caused by exposure of the skin to cigarette smoke, the cited combination of the '806 and Egawa, et al. reference likewise fails, as there would be no motivation to apply the claimed composition to the skin to prevent reduction in corneum moisture content and suppress ultraweak chemiluminescence in the skin, as called for in the claims herein.

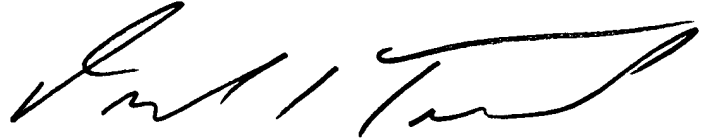
In view of the inapplicability of 2 of the 3 cited references as prior art, and the arguments concerning the '806 reference presented above, it is believed that the Examiner would now be justified in withdrawing the above rejection. Withdrawal of the rejection is accordingly respectfully requested.

In view of the foregoing, it is respectfully submitted that the application is now in condition for allowance, and early action and allowance thereof is accordingly respectfully requested. In the event there is any reason why the application cannot be allowed at the present time, it is respectfully requested that the Examiner contact the undersigned at the number listed below to resolve any problems.



Respectfully submitted,

TOWNSEND & BANTA

A handwritten signature in black ink, appearing to read 'Donald E. Townsend', written in a cursive style.

Donald E. Townsend  
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A handwritten signature in black ink, appearing to read 'Donald E. Townsend, Jr.', written in a cursive style.

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MARKED-UP VERSIONS OF AMENDED CLAIMS 1 AND 13:

1. (Amended) A method of treating environmental stress due to tobacco smoke by suppressing a reduction in corneum moisture content caused by contact with tobacco smoke comprising applying to the skin a liniment comprising (a) 0.001 to 5.0 wt% of sulfur containing amino acids selected from the group consisting of methionine, cystine, cysteine and glutathione; and

one or more ingredients selected from the group consisting of:

[0.001 to 5.0 wt% of sulfur containing amino acids selected from the group consisting of methionine, cystine, cysteine and glutathione;]

(b) 0.001 to 5.0 wt% of metabolic intermediates of sulfur containing amino acids, said metabolic intermediates selected from the group consisting of homocysteine, sulfinic acid, cysteinic acid, thiocysteine, taurine, thiotaurine, hypotaurine, djenkolic acid, cystathionine, S-allylcysteine, lanthionine and enthionine;

(c) 0.001 to 5.0 wt% of tannin; and

(d) 0.001 to 10.0 wt% of vitamin C and [its] derivatives thereof, said vitamin C and derivatives thereof selected from the group consisting of sodium ascorbate, L-ascorbic acid phosphoric ester, [selected from the group consisting of] L-ascorbic acid 2-phosphoric ester, L-ascorbic acid 3-phosphoric ester and DL- $\alpha$ -tocopherol-2-L-ascorbic acid diphosphoric ester, L-ascorbic acid-2-

sulfuric ester, L-ascorbic acid-3-sulfuric ester, and L-ascorbic acid glucoside.

13. (Amended) A method of treating environmental stress due to exposure of the skin to tobacco smoke by suppressing ultraweak chemiluminescence from the skin due to contact with tobacco smoke comprising applying to the skin a liniment comprising (a) 0.001 to 5.0 wt% of sulfur containing amino acids selected from the group consisting of methionine, cystine, cysteine and glutathione; and

one or more ingredients selected from the group consisting of:

[0.001 to 5.0 wt% of sulfur containing amino acids selected from the group consisting of methionine, cystine, cysteine and glutathione;]

(b) 0.001 to 5.0 wt% of metabolic intermediates of sulphur containing amino acids, said metabolic intermediates selected from the group consisting of homocysteine, sulfinic acid, cysteinic acid, thiocysteine, taurine, thiotaurine, hypotaurine, djenkolic acid, cystathionine, S-allylcysteine, lanthionine and enthionine;

(c) 0.001 to 5.0 wt% of tannin; and

(d) 0.001 to 10.0 wt% of vitamin C and [its] derivatives thereof, said vitamin C and derivatives thereof selected from the

group consisting of sodium ascorbate, L-ascorbic acid phosphoric ester, [selected from the group consisting of] L-ascorbic acid 2-phosphoric ester, L-ascorbic acid 3-phosphoric ester and DL- $\alpha$ -tocopherol-2-L-ascorbic acid diphosphoric ester, L-ascorbic acid-2-sulfuric ester, L-ascorbic acid-3-sulfuric ester, and L-ascorbic acid glucoside.